AGCAGAGAGCCTGGTGGGCATGGACATCTTTATCCACATACCTTAGTGTGAC
CACGCCGACAGAAAACTACTAAGGCCATCTCAGGGGTGCCTGTGCCAGGAGA
GGGGGGCGGTGTCCCCGGGCCGCAGAGCCATGCCTTTCGGCCTGAAGCTCCG
CAGGACTCGGCGCTACAACGTCCTGAGCAAGAACTGCTTTGTTGCCCGGATC
CGCCTGCTGGACAGCAATGTCATCGAGTGCACGCTGTCGGTGGAAAGCACGG
GGCAAGAGTGCCTGGAGGCCGTGGCCCAGAGGCTGGAGCTGAGGGAGACGC
ACTACTTCGGCCTTTGGTTTCTCAGCAAGAGCCAGCAGGCGAGATGGGTAGA
GCTGGAGAAGCCACTGAAGAAACATCTGGACAAGTTTGCTAACGAGCCTCTG
CTTTTCTTCGGAGTCATGTTCTATGTGCCAAATGTGTCACGGCTTCAGCAGGA
GGCCACAAGATATCAGTATTACCTGCAAGTCAAAAAAGACGTGCTTGAAGGA
CGGTTGCGGTGCTCCCTGGAACAAGTGATCCGGCTGGCTGGCTTAGCTGTGC
AAGCTGACTTCGGAGATTATAACCAGTTTGATTCCCAAGAGTTCCTCCGAGA
GTATGTGCTCTTTCCTATGGATTTGGCCATGGAGGAGGCGGCTCTGGAGGAG
CTAACCCAGAAGGTGGCCCAGGAACACAAAGCTCATAGCGGGATCCTGCCG
GCTGAAGCTGAACTGATGTACATCAACGAGGTAGAGCGTTTGGATGGATTTG
GACAGGAGATCTTCCCCGTGAAGGACAGTCATGGCAACAGCGTGCACCTCGG
CATCTTCTTCATGGGGATTTTTGTGAGGAACAGGGTCGGGAGACAGGCAGTG
ATATACAGGTGGAATGACATTGGGAGTGTTACTCACAGCAAAGCAGCCATCC
TGTTGGAGCTGATTGACAAGGAGGAGACCGCGCTCTTCCATACAGATGATAT
TGAAAATGCCAAGTACATTTCTCGGTTGTTTACCACTCGGCACAAATTTTACA
AACAGAACAAGATCTGCACTGAACAGTCAAATTCTCCACCCCCAATCAGACG
CCAGCCCACCTGGAGCCGGTCCTCACTGCCAAGGCAGCAGCCGTATATCTTG
CCTCCCATGCATGTCCAGTGCAGTGAGCACTACTCGGAGACCCATACTTCCCA
AGACAGCATTTTCCCCGGGAACGAAGAAGCCTTGTACTGCCGTTCTCACAAC
AGCCTGGACCTTAATTACTTGAACGGCACCGTCACCAATGGCAGCGTGTGCA
GCGTTCACAGCGTCAACTCCCTCAGCTGCTCCCAGAGCTTCATTCAGGCGTCT
CCAGTGTCCTCCAACCTTAGCATCCCTGGGAGTGACATCATGAGGGCCGATT
ACATCCCCAGCCACCGCCACAGCACCATCATCGTGCCGTCTTACAGGCCGAC
CCCAGATTACGAGACGGTCATGAGGCAGATGAAGAGGGGTCTGATGCACGC
AGACAGCCAGAGCCGGTCTCTGCGTAACCTCAATATCATCAACACCCATGCC
TATAACCAGCCCGAGGAACTGGTGTACAGCCAGCCGGAGATGCGGGAGAGG
CATCCCTACACGGTCCCCTATGCACACCAGGGGTGCTACGGTCACAAACTTG
TAAGTCCGTCTGACCAGATGAACCCCCAAAATTGTGCGATGCCTATCAAGCC
AGGGGCCAGTTCCATCTCTCACACAGTGAGCACTCCAGAACTAGCCAACATG
CAGCTCCAAGGAGCACAACACTATAGCACAGCCCACATGCTCAAGAACTATC
TATTCAGGCCGCCACCCCCTTACCCTCGGCCCCGTCCTGCCACCAGCACCCCA
GACCTCGCCAGCCACCGCCACAAGTACGTCAGCGGCAGCAGCCCTGATCTGG
TAACTCGGAAGGTGCAGCTCTCCGTAAAGACCTTCCAGGAGGACAGCTCACC
TGTGGTCCATCAGTCTCTGCAGGAGGTGAGCGAACCCCTCACAGCCACCAAG
CACCATGGCGGCGGCGGTGGCACGGTGAATAAACGCCACAGCCTGGAGGTG

FIGURE 1A

ATGAACAGCATGGTGAGAGGCATGGAGGCCATGACACTGAAGTCACTCAATA
TCCCCATGGCTCGCCGCAACACCCTTCGGGAGCAGGGCCCTTCCGAGGAGAC
GGGCGGCCACGAAGTGCACGGTCTCCCCCAGTATCACCACAAGAAGACATTC
TCGGATGCCACCATGCTGATCCACAGCAGTGAGAGCGAGGAAGAGGAGGAG
ACCCTGGAGGCTGCACCTCAGGTTCCTGTGCTTCGAGAGAAAGTAGAATACA
GTGCCCAGCTGCAGGCTGCCCTGGCCCGCATCCCCAACAGGCCCCCACCTGA
GTACCCAGGGCCAAGAAAAAGTGTCAGTAATGGGGCACTGAGACAGGACCA
GGGAACCCCTCTTCCTGCCATGGCCAGGTGCAGGGTGCTGAGACACGGACCA
TCCAAGGCCCTCAGTGTCTCCCGGGCAGAGCAGCTGGCTGTCAACGGTGCCT
CTCTGGGTCCCTCCATCTCTGAGCCTGACCTAACCAGCGTGAAGGAGCGGGT
CAAGAAAGAGCCTGTGAAGGAAAGGCCGGTGTCAGAGATGTTCTCCCTGGAG
GACAGCATTATAGAGAGAGAGATGATGATCAGGAATCTAGAGAAGCAGAAG
ATGACGGGCCCGCAGGCACAGAAGAGACCGCTGATGTTGGCAGCGCTGAAT
GGGCTCTCGGTGGCCCGAGTGTCGGGGCGGGAAGATGGTCGCCATGATGCCA
CCCGAGTCCCCATAGACGAGAGGCTCAGAGCCCTGAAGAAGAAGCTGGAAG
ATGGAATGGTGTTCACAGAATATGAGCAGATTCCAAACAAAAAGGCCAACG
GCGTCTTCAGCACCGCCACTCTGCCTGAGAACGCCGAGCGCAGCCGGATCCG
AGAAGTTGTCCCATATGAGGAGAATCGAGTGGAGCTCATCCCGACCAAAGAA
AACAACACAGGCTATATCAACGCCTCCCACATCAAGGTGGTGGTCGGCGGAT
CAGAATGGCACTACATCGCCACCCAGGGGCCCTTGCCACATACGTGCCATGA
CTTCTGGCAGATGGTGTGGGAGCAGGGGGTGAATGTGATCGCCATGGTCACT
GCAGAGGAGGAGGGTGGACGGACCAAAAGCCATCGATACTGGCCCAAACTG
GGGTCCAAGCATAGTTCTGCCACCTACGGCAAGTTCAAGGTCACCACAAAGT
TCCGGACAGATTCTGGTTGCTATGCAACGACGGGCCTAAAGGTGAAGCACCT
GCTGTCCGGGCAGGAGAGGACCGTGTGGCACTTGCAGTACACGGACTGGCCC
CACCACGGCTGTCCAGAAGACGTCCAAGGATTTTTGTCCTACTTGGAGGAAA
TCCAGTCAGTCCGACGCCACACCAACAGCGTGCTGGAAGGCATCAGGACCAG
GCACCCCCCCATCGTGGTTCACTGCAGCGCGGGTGTGGGAAGGACTGGTGTG
GTTATCCTCTCTGAGCTCATGATCTACTGCCTGGAACACAACGAAAAGGTGG
AGGTGCCCACGATGCTGCGATTCCTCAGGGAGCAGAGGATGTTCATGATCCA
GACCATTGCGCAGTACAAGTTCGTCTACCAAGTCCTCGTCCAGTTCCTGCAGA
ATTCCAGGCTCATTTGATCTCCTCCGGGATGCAGCTTCTGGAGGAGGGACGC
AGCTCTGTCCTGCAGGGGGCGGCCACTTCGACAACATCTGCCTCCCCCAGCC
AGAGGTGGATGGCTGGCAGCAGGCAGAAGCCAGAGTTACTCACAAACATCA
TGTATTATTTTATATAAGATAATTTATTTTTTTCCCTCTTTGGAATAAGTTCTG
TGAGTTATTATATAATGCTTCCCCCCCATACACACACACAATAATATAGTGCT
TCTCATTTG (SEQ ID NO:1)

FIGURE 1B

underlined = deleted in targeting construct

bold = sequence flanking Neo insert in targeting construct

AGCAGAGAGCCTGGTGGGCATGGACATCTTTATCCACATACCTTAGTGTGACCACGCCGA
CAGAAAACTACTAAGGCCATCTCAGGGGTGCCTGTGCCAGGAGAGGGGGGCGGTGTCCCC
GGGCCGCAGAGCCATGCCTTTCGGCCTGAAGCTCCGCAGGACTCGGCGCTACAACGTCCT
GAGCAAGAACTGCTTTGTTGCCCGGATCCGCCTGCTGGACAGCAATGTCATCGAGTGCAC
GCTGTCGGTGGAAAGCACGGGGCAAGAGTGCCTG**GAGGCCGTGGCCCAGAGGCTGGAGCT**
GAGGGAGACGCACTACTTCGGCCTTTGGTTTCTCAGCAAGAGCCAGCAGGCGAGATGGGT
AGAGCTGGAGAAGCCACTGAAGAAACATCTGGACAAGTTTGCTAACGAGCCTCTGCTTTT
CTTCGGAGTCATGTTCTATGTGCCAAATGTGTCACGGCTTCAGCAGGAGGCCACAAGATA
TCAGTATTACCTGCAAGTCAAAAAAGACGTGCTTGAAGGACGGTTGCGGTGCTCCCTGGA
ACAAGTGATCCGGCTGGCTGGCTTAGCTGTGCAAGCTGACTTCGGAGATTATAACCAGTT
TGATTCCCAAGAGTTCCTCCGAGAGTATGTGCTCTTTCCTATGGATTTGGCCATGGAGGA
GGCGGCTCTGGAGGAGCTAACCCAGAAGGTGGCCCAGGAACACAAAGCTCATAGCGGGAT
CCTGCCGGCTGAAGCTGAACTGATGTACATCAACGAGGTAGAGCGTTTGGATGGATTTGG
ACAGGAGATCTTCCCCGTGAAGGACAGTCATGGCAACAGCGTGCACCTCGGCATCTTCTT
CATGGGGATTTTTGTGAGGAACAGGGTCGGGAGACAGGCAGTGATATACAGGTGGAATGA
CATTGGGAGTGTTACTCACAGCAAAGCAGCCATCCTGTTGGAGCTGATTGACAAGGAGGA
GACCGCGCTCTTCCATACAGATGATATTGAAAATGCCAAGTACATTTCTCGGTTGTTTAC
CACTCGGCACAAATTTTACAAACAGAACAAGATCTGCACTGAACAGTCAAATTCTCCACC
CCCAATCAGACGCCAGCCCACCTGGAGCCGGTCCTCACTGCCAAGGCAGCAGCCGTATAT
CTTGCCTCCCATGCATGTCCAGTGCAGTGAGCACTACTCGGAGACCCATACTTCCCAAGA
CAGCATTTTCCCCGGGAACGAAGAAGCCTTGTACTGCCGTTCTCACAACAGCCTGGACCT
TAATTACTTGAACGGCACCGTCACCAATGGCAGCGTGTGCAGCGTTCACAGCGTCAACTC
CCTCAGCTGCTCCCAGAGCTTCATTCAGGCGTCTCCAGTGTCCTCCAACCTTAGCATCCC
TGGGAGTGACATCATGAGGGCCGATTACATCCCCAGCCACCGCCACAGCACCATCATCGT
GCCGTCTTACAGGCCGACCCCAGATTACGAGACGGTCATGAGGCAGATGAAGAGGGGTCT
GATGCACGCAGACAGCCAGAGCCGGTCTCTGCGTAACCTCAATATCATCAACACCCATGC
CTATAACCAGCCCGAGGAACTGGTGTACAGCCAGCCGGAGATGCGGGAGAGGCATCCCTA
CACGGTCCCCTATGCACACCAGGGGTGCTACGGTCACAAACTTGTAAGTCCGTCTGACCA
GATGAACCCCCAAAATTGTGCGATGCCTATCAAGCCAGGGGCCAGTTCCATCTCTCACAC
AGTGAGCACTCCAGAACTAGCCAACATGCAGCTCCAAGGAGCACAACACTATAGCACAGC
CCACATGCTCAAGAACTATCTATTCAGGCCGCCACCCCCTTACCCTCGGCCCCGTCCTGC
CACCAGCACCCCAGACCTCGCCAGCCACCGCCACAAGTACGTCAGCGGCAGCAGCCCTGA
TCTGGTAACTCGGAAGGTGCAGCTCTCCGTAAAGACCTTCCAGGAGGACAGCTCACCTGT
GGTCCATCAGTCTCTGCAGGAGGTGAGCGAACCCCTCACAGCCACCAAGCACCATGGCGG
CGGCGGTGGCACGGTGAATAAACGCCACAGCCTGGAGGTGATGAACAGCATGGTGAGAGG
CATGGAGGCCATGACACTGAAGTCACTCAATATCCCCATGGCTCGCCGCAACACCCTTCG
GGAGCAGGGCCCTTCCGAGGAGACGGGCGGCCACGAAGTGCACGGTCTCCCCCAGTATCA
CCACAAGAAGACATTCTCGGATGCCACCATGCTGATCCACAGCAGTGAGAGCGAGGAAGA

FIGURE 2A

GGAGGAGACCCTGGAGGCTGCACCTCAGGTTCCTGTGCTTCGAGAGAAAGTAGAATACAG
TGCCCAGCTGCAGGCTGCCCTGGCCCGCATCCCCAACAGGCCCCCACCTGAGTACCCAGG
GCCAAGAAAAAGTGTCAGTAATGGGGCACTGAGACAGGACCAGGGAACCCCTCTTCCTGC
CATGGCCAGGTGCAGGGTGCTGAGACACGGACCATCCAAGGCCCTCAGTGTCTCCCGGGC
AGAGCAGCTGGCTGTCAACGGTGCCTCTCTGGGTCCCTCCATCTCTGAGCCTGACCTAAC
CAGCGTGAAGGAGCGGGTCAAGAAAGAGCCTGTGAAGGAAAGGCCGGTGTCAGAGATGTT
CTCCCTGGAGGACAGCATTATAGAGAGAGAGATGATGATCAGGAATCTAGAGAAGCAGAA
GATGACGGGCCCGCAGGCACAGAAGAGACCGCTGATGTTGGCAGCGCTGAATGGGCTCTC
GGTGGCCCGAGTGTCGGGGCGGGAAGATGGTCGCCATGATGCCACCCGAGTCCCCATAGA
CGAGAGGCTCAGAGCCCTGAAGAAGAAGCTGGAAGATGGAATGGTGTTCACAGAATATGA
GCAGATTCCAAACAAAAAGGCCAACGGCGTCTTCAGCACCGCCACTCTGCCTGAGAACGC
CGAGCGCAGCCGGATCCGAGAAGTTGTCCCATATGAGGAGAATCGAGTGGAGCTCATCCC
GACCAAAGAAAACAACACAGGCTATATCAACGCCTCCCACATCAAGGTGGTGGTCGGCGG
ATCAGAATGGCACTACATCGCCACCCAGGGGCCCTTGCCACATACGTGCCATGACTTCTG
GCAGATGGTGTGGGAGCAGGGGGTGAATGTGATCGCCATGGTCACTGCAGAGGAGGAGGG
TGGACGGACCAAAAGCCATCGATACTGGCCCAAACTGGGGTCCAAGCATAGTTCTGCCAC
CTACGGCAAGTTCAAGGTCACCACAAAGTTCCGGACAGATTCTGGTTGCTATGCAACGAC
GGGCCTAAAGGTGAAGCACCTGCTGTCCGGGCAGGAGAGGACCGTGTGGCACTTGCAGTA
CACGGACTGGCCCCACCACGGCTGTCCAGAAGACGTCCAAGGATTTTTGTCCTACTTGGA
GGAAATCCAGTCAGTCCGACGCCACACCAACAGCGTGCTGGAAGGCATCAGGACCAGGCA
CCCCCCCATCGTGGTTCACTGCAGCGCGGGTGTGGGAAGGACTGGTGTGGTTATCCTCTC
TGAGCTCATGATCTACTGCCTGGAACACAACGAAAAGGTGGAGGTGCCCACGATGCTGCG
ATTCCTCAGGGAGCAGAGGATGTTCATGATCCAGACCATTGCGCAGTACAAGTTCGTCTA
CCAAGTCCTCGTCCAGTTCCTGCAGAATTCCAGGCTCATTTGATCTCCTCCGGGATGCAG
CTTCTGGAGGAGGGACGCAGCTCTGTCCTGCAGGGGGCGGCCACTTCGACAACATCTGCC
TCCCCCAGCCAGAGGTGGATGGCTGGCAGCAGGCAGAAGCCAGAGTTACTCACAAACATC
ATGTATTATTTTATATAAGATAATTTATTTTTTTCCCTCTTTGGAATAAGTTCTGTGAGT
TATTATATAATGCTTCCCCCCCATACACACACACAATAATATAGTGCTTCTCATTTG

FIGURE 2B

Gene Sequence Structure *

192 bp Sequence Deleted 274 bp

Size of full-length cDNA: 3957 bp

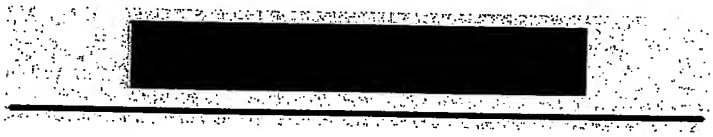
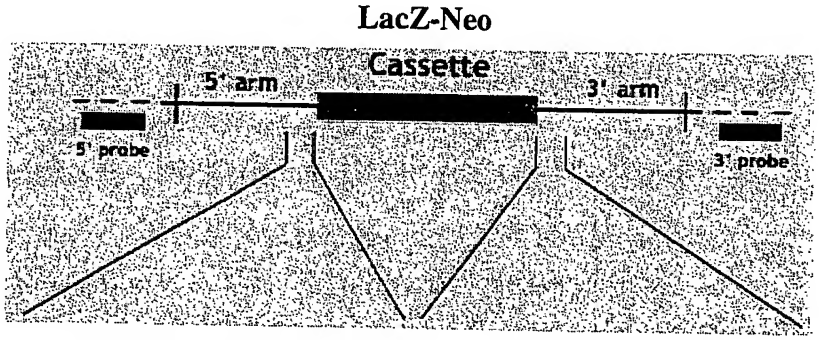


FIGURE 3

Targeting Vector* (genomic sequence)



Arm Length:
5': 3.5 kb
3': 2 kb

Targeting Vector
Endogenous Locus

* Not drawn to scale

5'>CAGCTGCCCGGCAGAGAGCCT GGTGGGCATGGACATCTTTATCCA CATACCTTAGTGTGACCACGCCGA CAGAAAACTACTAAGGCCATCTCA GGGGTGCCTGTGCCAGGAGAGGGG GGCGGTGTCCCCGGGCCGCAGAGC CATGCCTTTCGGCCTGAAGCTCCG CAGGACTCGGCGCTACAACGTCCT GAGCAAGAACT<3' (SEQ ID NO:2)

5'>GAGGCCGTGGCCCAGAGGCTG GAGCTGAGGGAGGTGAGTTGAGCG CGCATCCCTGCCTGTTGTGTGGAC AGGGAGTGGGCTCTTCAGAGGAAC CAGCTATCTGCTTAACGTGTTGGC ACCTGCTGTGTTTTCAGCCTAAGC GTGTGTTTAAAAGAACCTGCTTTT CTTAGGGTGGGTGTGGCCCGGGGA AGTTCCAGCAT<3' (SEQ ID NO;3)

FIGURE 4